Ratio of Maximum Coronary Flow Reserve in Response to Adenosine Compared to Baseline Coronary Flow Reserve		
Ratio of Maximum Coronary Blood Flow in Response to Acetylcholine Compared to Baseline Coronary Blood Flow	**Abnormal Ratio (≤2.5)**	**Normal Ratio (>2.5)**
Abnormal Ratio (≤1.5)	Coronary flow reserve: 2.3 (2.1-2.4)	Coronary flow reserve: 3.0 (2.8-3.5)
	Coronary blood flow: 0.9 (0.6-1.2)	Coronary blood flow: 1.0 (0.7-0.8)
	n=268	n=478
Normal Ratio (>1.5)	Coronary flow reserve: 2.2 (2.0-2.4)	Coronary flow reserve: 3.2 (2.9-3.7)
	Coronary blood flow: 2.0 (1.7-2.1)	Coronary blood flow: 2.2 (1.8-2.8)
	n=173	n=520

TCT-315

Invasively Derived Coronary Flow Capacity: Prognostic Implications of a Cross-modality Physiological Concept

Tim P. van de Hoef[1], Mauro Echavarria-Pinto[2], Martijn A. van Lavieren[3], M. Meuwissen[4], Patrick W. Serruys[5], Javier Escaned[6], Jan Piek[7]
[1]Academic Medical Center - University of Amsterdam, Amsterdam, Noord Holland, [2]Hospital Universitario Clinico San Carlos, Madrid, Spain, [3]Academic Medical Center, Amsterdam, Noord Holland, [4]Amphia Hospital, Breda, Netherlands, [5]Thoraxcenter, Rotterdam, MD, [6]Hospital Clinico San Carlos, Madrid, Spain, [7]Academic Medical Center, Amsterdam, Netherlands

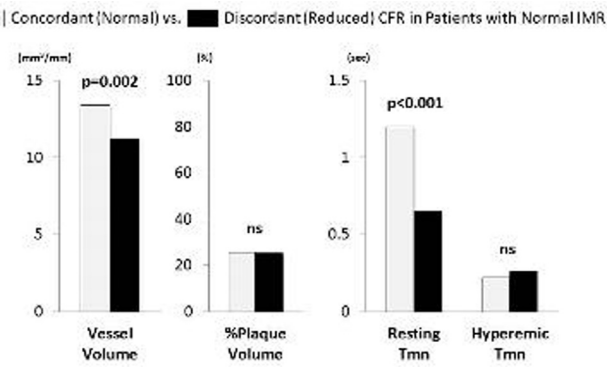
Background: Either coronary flow reserve (CFR) or fractional flow reserve (FFR) can suffice for diagnosis of significant coronary stenoses, but they can over- or underestimate severity in many cases. An alternative approach is the coronary flow capacity (CFC) concept, originally derived from PET-imaging, which integrates CFR and hyperemic flow (hAPV) to depict the ischemic burden of the myocardium. We studied the prognostic implications of addition of hAPV to CFR within the CFC concept derived from invasive measurements.
Methods: Coronary pressure and flow velocity were measured in 154 patients in whom revascularization was deferred in the pre-FAME era. The additive value of hAPV to CFR was tested with the net reclassification index (NRI), integral discrimination improvement (IDI) and relative IDI. After stratification in normal, mildly reduced, moderately reduced, and severely reduced CFC, using literature-derived CFR cut-offs and the corresponding hAPV percentiles, event rates up to 10-years follow-up were estimated with the Kaplan Meier method, and a Cox proportional hazards model was used to test the association of CFC with MACE, adjusting for confounding variables (p< 0.1).
Results: Median follow-up was 11.9 years (10.0 – 13.4 years). CFR was significantly associated with MACE (p< 0.001). The addition of hAPV to CFR yielded an NRI of 0.49 (Standard error (SE) 0.17, p=0.003), IDI of 0.024 (SE 0.012, p=0.04), and rIDI of 43.3%. In contrast, addition of FFR to CFR did not improve discrimination. KM-estimates of MACE across the CFC categories showed a significant linear trend at all time-points (P< 0.001), with MACE increasing with increasing impairment of CFC. After adjusting for confounding variables, CFC was strongly associated with long-term MACE: compared with normal CFC, a mildly and moderately reduced CFC were associated with a 1.9-fold (95% CI: 1.0 – 3.4, p=0.040), and a 2.8-fold (95% CI: 1.2 – 6.2, p=0.013) increase in MACE, respectively.
Conclusions: The addition of hAPV to CFR in the CFC concept improves its the discriminative value for MACE. CFC may provide a disruptive physiological concept, applicable to all diagnostic modalities that measure flow.

TCT-316

Impact of Coronary Artery Size on Physiologic Microcirculatory Indices: A Volumetric Intravascular Ultrasound Study with Coronary Flow Assessment

Yuhei Kobayashi[1], Yasuhiro Honda[1], William F. Fearon[1], Shigemitsu Tanaka[1], Peter Fitzgerald[1], Alan Yeung[1], Jennifer A. Tremmel[1]
[1]Stanford University, Stanford, United States

Background: Microvascular dysfunction has been associated with increased mortality. However, little is known whether physiologic microcirculatory indices can fundamentally be affected by coronary dimensions.
Methods: Volumetric IVUS (50 mm length) and physiologic assessment (Fractional Flow Reserve [FFR], Coronary Flow Reserve [CFR], and Index of Microcirculatory Resistance [IMR]) in the LAD artery were performed in 122 patients with non-obstructed epicardial arteries. Coronary flow was assessed with a thermo-dilution method by obtaining mean transit time (Tmn: an inverse correlate to absolute flow) at rest and hyperemia. IMR was measured as distal coronary pressure x hyperemic Tmn.
Results: No patient had significant stenosis in LAD (FFR: 0.87±0.04, %plaque volume: 26.1±9.0%). Resting Tmn positively correlated with vessel and lumen volumes (p< 0.01, p=0.04), whereas hyperemic Tmn showed no correlation with the artery size. As a result, IMR was unrelated to any IVUS indices, while CFR positively correlated with the artery size (p< 0.001 for both vessel and lumen). With microvascular dysfunction defined as IMR ≥25, ROC analysis determined CFR=3.75 as the best cutoff. Discordance of reduced CFR with normal IMR was seen in patients with smaller artery size, leading to shorter resting Tmn, despite the equivalent % plaque volume and hyperemic Tmn (Figure).



Conclusions: Small coronary size may increase resting coronary flow, reducing CFR even in the absence of epicardial stenosis and microvascular dysfunction. Potential impact of artery size should be noted in interpretation of physiologic indices using resting flow status.

TCT-317

Systematic detection of coronary vasospasm by methylergonovine-based provocative test in 2,397 patients

Helene Aelion[1], Julien Rosencher[1], Marie Caroline Chenilleau[1], Stephane Manzo-Silberman[2], Philippe Allouch[1], Arnaud Jegou[1], Naim Bouazza[1], Alain Cariou[1], Olivier Varenne[1]
[1]Hôpital Cochin, Paris, France, [2]Hopital Lariboisière, Paris, France

Background: In the absence of clear-cut indications for provocative test (PT), coronary artery spasm (CAS) may be underdiagnosed whereas the widespread use of early coronary angiography has found that acute ischemic syndromes are not always related to atherosclerotis. The objective of the present study was to evaluate the incidence of CAS in a population of patients with chest pain who underwent methylergonovine-based PT.
Methods: The present study is a retrospective analysis from an University tertiary care hospital where a policy of systematic detection of CAS by PT is applied in patients with chest pain at rest and without significant coronary stenosis. PT complications include death, MI, stroke, delayed or resistant CAS, ventricular fibrillation, and acute atrio ventricular block.
Results: During a 10-year period (2002-2012), a total of 18,454 angiographies were performed. CAS was documented in 256 (10.7%) of the 2,397 patients with normal or near normal coronary arteries and chest pain who underwent PT. Compared to the overall population, CAS patients were more often female (44.7% vs. 29.6%; p< 0.0001), younger (55 [47.5-64] years vs. 61 [52-70] years; p=0.0001), and smokers (63.7% vs. 42.3%; p< 0.0001). Initial presentation was more frequently acute coronary syndrome (36.7% vs. 29.1%) or non-specific chest pain (46% vs. 21.9%). The rate of complications after PT was 0.9% (n=23). Complications included delayed or persistant CAS (0.3%), VF/asystoly/AVB (0.3%), transient ischemic attack (0.2%), and non Q wave MI (0.04%). Urgent coronary stenting was required to restore arterial patency in three patients with persistant CAS.
Conclusions: This retrospective study of 10 years of experience suggests that CAS is present in 10.7% of patients with myocardial ischemia symptoms at rest and without significant coronary stenosis. Methylergonovine based PT appear to be extremly safe when performed in selected patients with normal or near normal coronary arteries. These findings could justify performing PT more systematically in this setting to avoid the potentially severe outcomes of undiagnosed CAS.

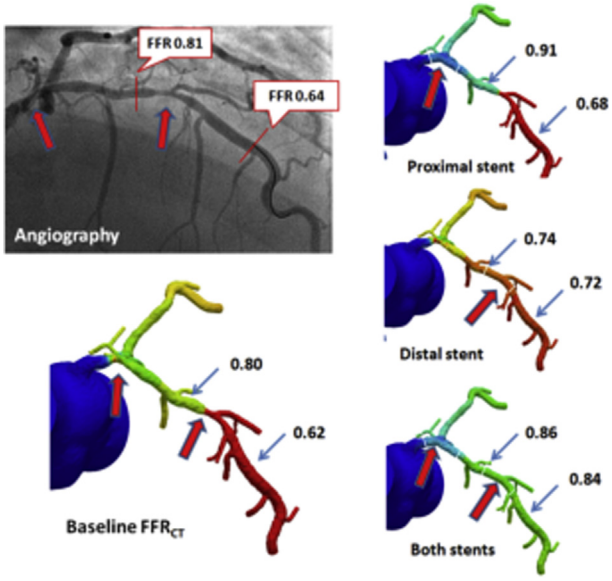
TCT-318

Trans-lesional FFRCT gradient correlates with measured FFR gradient in vessels with serial coronary stenosis: role in stenting strategy

Kentaro Tanaka[1], Hiram Bezerra[1], Hans Erik Botker[2], Bjarne Nørgaard[2]
[1]Harrington Heart and Vascular Institute, Case Medical Center, Cleveland, OH, [2]Aarhus University Hospital, Skejby, Denmark

Background: Fractional flow reserve derived from coronary CT (FFRct) has high diagnostic accuracy compared to FFRcath, and modulation of the FFRct with "virtual

stenting" is feasible for predicting the effect of PCI. However, the validity of FFRct along the length of a vessel compared with FFRcath is unknown. The purpose of this study is to compare trans-lesional FFRcath vs. FFRct gradients in vessels with serial stenoses.
Methods: 18 patients with stable coronary artery disease had pull-back FFRcath measurements across the serial lesions. In each patient FFRct was performed utilizing pre-cath cCTA data. Blinded comparisons of FFRcath and FFRct at co-registered points were performed. Computational models were then modified to simulate virtual stenting strategy of the proximal, distal or both lesions.
Results: 18 vessels were assessed, with ischemia (FFRcath $\leq$0.80) present in 13 (72.2%). Each patient had 2 or more angiographic stenoses >30% with trans-lesional FFRcath gradient of 0.10±0.09. The correlation between FFRcath and FFRct gradient was r=0.92, p< 0.001. Virtual stenting demonstrated a wide range of scenarios with the need for one or two stents for relief of the ischemia. Figure 1 exemplifies a case in which stenting of each single lesion did not result in FFRct >0.8. Virtual stenting of both stenoses relieved the ischemia with final FFRct = 0.84.
Conclusions: Trans-lesional FFRct gradient correlates closely with FFRcath gradient in vessels with serial stenoses. This is a core foundation for the potential usefulness of computational modeling to evaluate and plan treatment of complex and serial stenoses.

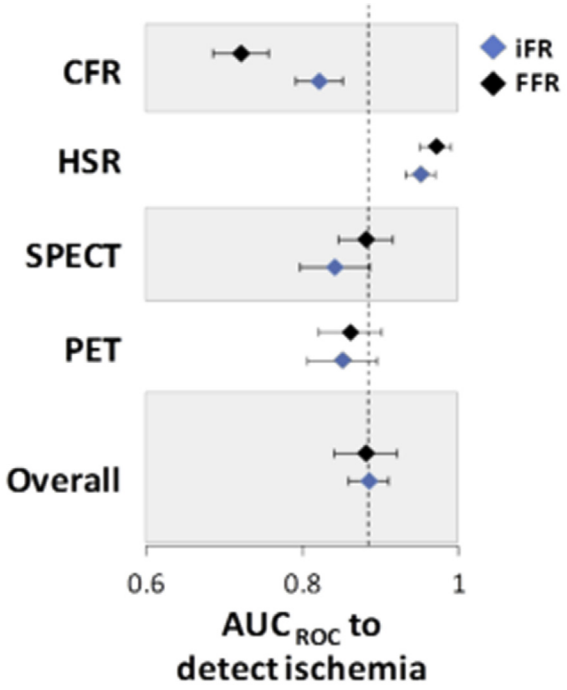


TCT-319

Instantaneous wave-free ratio (iFR) and fractional flow reserve (FFR) are equally able to identify ischaemia and flow limitation: a pooled analysis of studies against SPECT, HSR, CFR and PET

Ricardo Petraco[1], Sukhjinder S. Nijjer[2], Sayan Sen[3], Guus A. de Waard[4], Tim P. van de Hoef[5], Mauro Echavarria-Pinto[6], Rasha Al-Lamee[7], Martijn A. van Lavieren[8], Paul Knaapen[9], Javier Escaned[10], Jan Piek[11], Niels van Royen[9], Justin E. Davies[3]
[1]Imperial College, London, United Kingdom, [2]Imperial College London, London, London, [3]Imperial College London, London, United Kingdom, [4]VU University Medical Center, AMSTERDAM, Netherlands, [5]Academic Medical Center - University of Amsterdam, Amsterdam, Noord Holland, [6]Hospital Universitario Clinico San Carlos, Madrid, Spain, [7]IMPERIAL COLLEGE NHS TRUST, LONDON, LONDON, [8]Academic Medical Center, Amsterdam, Noord Holland, [9]VU University Medical Center, Amsterdam, Netherlands, [10]Hospital Clinico San Carlos, Madrid, Spain, [11]Academic Medical Center, Amsterdam, Netherlands

Background: The instant wave-free ratio (iFR) and fractional flow reserve (FFR) are indices of coronary disease severity which use pressure as a measure of lesion significance. The aim of this study was to quantify iFR and FFR's individual ability to detect ischaemia and flow limitation against multiple perfusion modalities.
Methods: Pooled analysis of data using a random effect model. 4 studies which compared iFR and FFR against the following perfusion modalities were included: SPECT scintigraphy, positron emission tomography (H215O PET), hyperaemic stenosis resistance (HSR) and coronary flow reserve (CFR). In total, 265 stenoses in 220 patients were evaluated. The performance of iFR and FFR to detect ischaemia or flow limitation was compared using the area under the ROC curve (AUCROC).
Results: Baseline iFR and hyperaemic FFR demonstrated equal overall agreement with methods of perfusion (iFR AUCROC=0.88, FFR AUCROC=0.88) (Figure). When non-invasive perfusion methods were used as reference standards, iFR was non-inferior to FFR (iFR-SPECT AUCROC=0.84 vs FFR-SPECT AUCROC=0.88, p>0.2; iFR-PET AUCROC=0.85, FFR-PET AUCROC=0.86, p>0.2). When invasive flow indices were used as reference comparisons, iFR was non-inferior (iFR-HSR AUCROC=0.95 vs FFR-HSR AUCROC=0.97, p>0.3) or superior to FFR (iFR-CFR AUCROC = 0.82 vs FFR-CFR AUCROC=0.72, p< 0.01) to detect flow limitation.



Conclusions: iFR and FFR are equally able to detect ischaemia and flow limitation, against multiple perfusion modalities. Studies with hard clinical endpoints will evaluate whether the non-inferiority of iFR will translate into favourable clinical outcomes.

TCT-320

Outcomes of Fractional Flow Reserve Guided Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting in Left Main or Triple Vessel Disease

Jung-Min Ahn[1], Hee-Soon Park[1], Se Hun Kang[1], Sang Soo Cheon[1], Byeong Joo Bae[1], Min Su Kim[1], Jae Hyung Roh[1], Hyun Woo Park[1], Mineok Chang[1], Sung-Han Yoon[1], Jong-Young Lee[1], Duk-Woo Park[1], Soo-Jin Kang[1], Seung-Whan Lee[1], Young-Hak Kim[1], Cheol Whan Lee[1], Seong-Wook Park[1], Seung-Jung Park[1]
[1]Asan Medical Center, Seoul, Korea, Republic of

Background: To compare the clinical outcomes of fractional flow reserve (FFR) guided percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG) in left main or triple vessel disease.
Methods: Between January 2008 and December 2011, a total of 1515 patients with significant left main or triple vessel disease received FFR guided PCI (N=250) or CABG (N=1265). Primary endpoint was the composite of death from any cause, myocardial infarction (MI), stroke, or repeated revascularization (MACCE) at 1 year.
Results: At 1 year follow-up, MACCE occurred 12 (4.8%) in FFR guided PCI group and 61 (4.8%) in CABG group (P=0.97). The rate of death were similar between groups (3 [1.2%] vs. 37 [2.9%], P=0.12). The rate of the composite of death, MI or stroke was significantly lower in FFF-guided PCI group (3 [1.2%] vs. 51 [4.0%], P=0.029). The rate of repeated revascularization was significantly lower in CABG group (9 [3.6%] vs. 13 [1.0%], P=0.002). After adjustment, the risk of MACCE at 1 year was not significantly different between groups (hazard ratio [HR] 0.99, 95% confidence interval [CI] 0.54-1.85, p=0.99). The risk of death was not significantly different (HR 0.40, 95% CI 0.14-1.34, P=0.13). The risk of the composite of death, MI, or stroke was significantly lower in FFR guided PCI group (HR 0.30, 95% CI 0.09-0.96, P=0.042) and the risk of repeated revascularization was significantly lower in CABG group (HR 3.18, 95% CI 1.35-7.50, P=0.008).